UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/061,979	01/31/2002	Jeremy S. Lee	080129-000100US	2049

20350 7590 11/30/2004

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/061,979	LEE ET AL.	
	Examiner	Art Unit	
	Maria B Marvich, PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to an amendment and Declaration under Rule 132 by Dr. van Drunen Littel-van den Hurk filed 9/14/04. The Declaration has been considered. Claim 5 is withdrawn. Clams 3 and 16 have been amended. Claim 1-4 and 6-22 are under examination in this office action.

Response to Amendment

Any rejection of record in the previous action not addressed in this office action is withdrawn. There are new grounds of rejection herein that were not necessitated by applicants' amendment and therefore, this action is not final.

Claim Objections

1. Claims 1, 6-14 and 18-22 are objected to because of the following informalities: the claims are drawn to non-elected subject matter. Applicants have elected a method of producing an immune response while the claims read broadly on any physiological response, which includes non-elected subject matter. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection.**

Claims 4 and 17 are vague and indefinite in that the metes and bounds of an "immune response produces antibodies" are unclear. The immune response is a response to foreign epitopes or antigenic determinants that results in a series of events of which one is the production of antibodies. However, the immune response itself does not "produce" antibodies. Specialized cells produce the antibodies during the immune response.

Claims 1, 6-14 and 18-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing antibodies in response to M-DNA, does not reasonably provide enablement for a method of producing a physiological response such as an therapeutic immune response. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. **This is a new rejection.**

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and In *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

1) **Nature of invention**. The invention recites a method of producing a physiological response using metal containing nucleic acid comprising two strands of nucleic acid, which are joined by hydrogen bonds and interchelated with divalent metal cations or M-DNA. M-DNA has the properties of electrical conductance as well as being nuclease resistant. Therefore, introduction of the nuclease resistant M-DNA can result in prolonged response *in vivo*. The invention utilizes a combination of molecular biology and clinical techniques.

2) **Scope of the invention**. Base claim 1 recites a method of producing a physiological response by administering metal containing nucleic acid, which reads on a method of gene therapy. Specifically in claims 3-4 and 16-17, the physiological response upon M-DNA introduction into an animal is the induction of an immune response. While applicants have provided guidance for the production of antibodies in animals using M-DNA in the specification and in a Declaration filed 9/14/04, applicants have not provided an enabling disclosure for the broad and diverse class of all physiological responses including an immune response. The lack of guidance for the induction of physiological responses or therapeutic immune responses exacerbates, or makes worse, an unpredictable method of producing a physiogical response with M-DNA.

3) **Number of working examples and guidance**. The specification teaches construction of metal containing nucleic acids in which divalent metal cations such as Ni^{2+}, Co^{2+} and Mg^{2+} are interchelated with the hydrogen bonded base pairs and coordinated to a nitrogen atom of the aromatic bases. The metal containing nucleic acid has the property of electrical conductance by accepting electrons from an electron donor. M-DNA is proposed to be useful in detection systems for the identification of PCR products, ligation reactions, for the detection of particular

genomic sequences and to monitor presence of nucleic acid binding moieties in a sample. Furthermore, M-DNA is nuclease resistant and therefore applicants propose its use in M-DNA to mediate physiological response *in vivo* such as to generate an immune response. Applicants demonstrate that the M-DNA is immunogenic by injecting Ni^{2+} containing M-DNA intraperitoneally into Balb/C mice. Mice immunized with M-DNA show antibody titres to M-DNA. The disclosure neither provides examples of using M-DNA to express antigenic protein nor teaches that the DNA specifically disclosed in example 1 and used in examples 2-4 would transcribe normally. Without knowing the nature of the DNA, the ability to generate an immune response is highly unpredictable.

4) **State of Art**. A brief survey of the art reveals that a physiological response is any of a number of diverse and unrelated responses such as emotional, biochemical, physical and immunogenic. Immune responses include a myriad of effects including the production of antibodies. In the instant disclosure, it appears that the nature of the physiological response is determined by coding sequences delivered by the M-DNA. However, applicants do not disclose any specific DNA coding sequence nor the correlations between products and response except to disclose that antibodies are generated in response to injection of M-DNA. The response is directed against the M-DNA in this case but not against any specific disclose epitope. Typically, the DNA encodes an antigenic determinant to which an immune response is mounted by the host system (Falo et al pages 1239-1240). The art of producing any of a number of physiological responses without knowing the target or without knowing what DNA is to be used.

5) **Unpredictability of the art**. The specification discloses that BalbC mice are injected with M-DNA. Applicants provide a Declaration in which they demonstrate that tgD DNA

encoded by M-DNA is expressed. Furthermore, introduction of the M-DNA into mice resulted in an increase in tgD-specific IgG titre as determined by an ELISA. While an immune response would be anticipated from injection of M-DNA either as evidenced by the production of antibodies to M-DNA as demonstrated in the specification or to an antigenic epitope encoded by the M-DNA, the production of any immune response by undisclosed DNA is highly unpredictable. By reciting any physiological response produced upon administration of an M-DNA, the unpredictability of the invention is high. The specification lacks disclosure as to the nature of the physiological response and methods of producing these responses aside from immunogenic related methods. In addition, the nucleic acid is completely unknown at the onset as the invention. Therefore, the unpredictability of using the claimed invention for production of physiological responses is mitigated due to the lack of methods or processes disclosed in the specification.

6) **Summary**. The invention recites a method for the production of a physiological response in animals by administration of metal containing nucleic acids. In view of unpredictability of the art to which the invention pertains and the lack of established protocols and the inability to predict what physiological response is sought, the broad and diverse nature of physiological responses and the lack of disclosure as to DNA to be used to elicit the responses: undue experimentation would be required to practice the claimed methods with reasonable expectation of success, absent a specific and detailed description in the specification. Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be concluded that the skilled artisan would have

had to have conducted undue, unpredictable experimentation in order to practice the claimed invention.

Response to Argument

Applicants traverse the claim rejections under 35 U.S.C. 112, first paragraph on pages 9-11 of the amendment filed 9/14/04 and in the Declaration by Dr. Sylvia van den Hurk filed 9/14/04. Essentially, Applicants arguments and the Declaration argue the following. 1) The invention does not embrace gene therapy rather several methods are disclosed including methods and compositions for injection of M-DNA for expression of a desired product. 2) Dr. Van der Hurk has conducted experiments that demonstrate that M-DNA which encodes an antigenic protein can be expressed in animals and the expressed protein elicits an immune response. The immune response is indicated by production of IgG. 3) The art of DNA vaccines is quite well developed as evidenced by the number of patents.

Applicants' arguments filed 9/14/04 have been fully considered but they are not persuasive. Applicants' claims are directed at the injection of DNA into an animal for the production of a protein. Specifically, antigenic determinants are produced to which antibodies are produced. However, applicants' claims are directed to a broader application that encompasses gene therapy. As evidenced by the Rule 132 Declaration by Dr. van der Hurk, the applicants have only demonstrated that upon injection of M-DNA encoding antigenic determinants, antibodies are produced. As applicants have argued, the art of producing vaccines is well established. However, the broad recitation of methods or producing a physiological

response and even a method of producing a therapeutic immune response by injection of M-DNA is not supported by the specification or the art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1636

March 4, 2004

GERRY LEFFERS
PRIMARY EXAMINER